

### **Remarks/Arguments**

Upon entry of the amendments made herein, claims 1, 4, 29-36, 42, 43, 49-62, 66-82, 84 and 85 are pending in the application. By this amendment, Applicants have amended claims 1, 4, 29, 31, 32, 34-36, 42, 50, 52-55, 60, 62, 67, 69, 71-75, 77, 80 and 81. Claim 3 is canceled herein without prejudice or disclaimer. Claims 2, 5-28, 37-41, 44-48, 63-65, 83, 86 and 87 were previously canceled.

Claims 1, 29, 35, 36, 50, 67, 69, 71 and 81 have been amended to further define the invention. Claims 4, 31, 32, 34, 42, 52-55, 60, 62, 72-75, 77 and 80 have been amended to correct inadvertent typographical errors, to maintain proper antecedent basis and/or to maintain proper claim dependencies. Accordingly, no new matter has been added.

### **Formal Matters**

Applicants note that Table 1 in the instant published application, U.S. Application No. 20040242548, includes several compounds with incomplete structures. Therefore, Applicants have herewith provided Table 1, in the Amendments to the Specification, with each structure enlarged for clarity.

As acknowledged by the Examiner, Applicants have previously elected Group I (*i.e.*, aryl represents furanyl and benzofuranyl). (*See* Office Action at p. 19). Applicants also note the Examiner's statement to allow the joinder of Group III (*i.e.*, aryl represents benzothienyl) following Applicants' response. (*See* Office Action at pp. 19-20). In view of the amendments herein, Applicants request the joinder of group III (*i.e.*, aryl represents benzothienyl) as well as the thienyl moiety with elected Group I.

Applicants further note that, contrary to the Examiner's assertion, the definition of R<sup>7</sup> in claim 1 allows for substituted furanyl, substituted benzofuranyl, substituted thienyl and substituted benzothienyl groups. (*See* Office Action at p. 20). In fact, these aryl groups can be substituted at one or more ring positions. *See e.g.*, page 87, lines 4-26 of the application as filed. In an effort to further prosecution, the definition of R<sup>7</sup> in claims 1, 67, 69 and 81 has been amended to specifically include substituted furanyl, substituted benzofuranyl, substituted thienyl and substituted benzothienyl groups. Thus, the elected species is encompassed by the pending claims.

Finally, Applicants herein provide the following list of co-pending applications which include descriptions of general formulae including the claimed multicyclic structure, ring substituents (*i.e.*, R<sup>2</sup>, R<sup>2'</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>8</sup>, R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup>), heteroaryl group(s) at the 7-position and hydrogen at the 9-position. By submitting this list, the Applicant makes no representation that: (1) a search has been performed, of the extent of any search performed, or that more relevant information does not exist; (2) the information cited in the patents/applications below is, or is considered to be, material to patentability as defined in 37 C.F.R. §1.56(b); and (3) the information cited in the patents/applications below is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102. Notwithstanding any statements by the Applicant, the Examiner is urged to form his/her own conclusion regarding the relevance of the cited information.

U.S. Application No./ U.S. Patent No.	Attorney Docket No.
5,589,470	16534-502001US
5,811,412	16534-502C01US
6,756,365	16534-502C03US
7,414,041	16534-502C04US
12/194,362	16534-502C05US
6,617,318	16534-510001US
11/004,559	16534-510C02US
11/390,902	16534-510C03US
7,067,681	16534-510D01US
6,833,365	16534-511001US
7,202,235	16534-511C01US
11/728,346	16534-511C02US
6,642,270	16534-513001US
11/305,048	16534-513C02US
11/974,019	16534-513C03US
6,818,635	16534-518001US
10/853,635	16534-518C01US
6,624,168	16534-520001US
7,094,806	16534-520C02US
7,361,674	16534-520C03US
12/074,466	16534-520C04US
6,841,546	16534-524001US
7,045,507	16534-525001US
10/943,571	16534-525C01US
10/692,563	16534-526002US (Instant case)
10/996,119	16534-528C01US
7,056,902	16534-532001US
11/283,571	16534-532C01US
7,001,918	16534-535C03US
11/292,552	16534-535C04US
10/740,961	16534-536C01US
11/069,197	16534-538C02US
10/692,764	16534-539001US
10/877,928	16534-541001US
11/258,622	16534-545001US
11/348,608	16534-547001US

11/657,412	16534-549001US
11/803,854	16534-550001US
11/870,317	16534-552001US
11/963,509	16534-553001US
11/963,540	16534-554001US
12/102,623	16534-556001US
12/110,627	16534-557001US
12/423,718	16534-564001US
61/098,594	16534-569P01US
61/108,386	16534-569P02US
61/156,679	16534-570P01US

### 35 U.S.C. §112

Claims 1, 3, 4, 29-36, 42, 43, 49-62, 66-82, 84 and 85 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

The Examiner stated that the term “prodrug moiety” does not include sufficient written description in the instant specification. (See Office Action at pp. 5-6).

Applicants traverse the rejection. However, in an effort to further prosecution, the term “prodrug moiety” has been deleted from the current claims. Accordingly, Applicants believe the rejection has been overcome and reconsideration is requested.

Claims 1, 3, 4, 29-36, 42, 43, 49-62, 66-82, 84 and 85 have been rejected under 35 U.S.C. §112, first paragraph, as lacking enablement.

Claims 1, 67, 69 and 81 have been amended to recite the following R groups:

$R^2$  and  $R^{2'}$  are each hydrogen;

$R^{4'}$  and  $R^{4''}$  are each alkyl;

$R^4$  is  $NR^{4'}R^{4''}$ ;

$R^3$ ,  $R^{11}$  and  $R^{12}$  are each hydrogen;

$R^{10}$  is hydrogen;

$R^5$  is hydroxyl, hydrogen or thiol;

$R^6$  and  $R^{6'}$  are independently hydrogen hydroxyl, thiol or alkyl;

$R^7$  is substituted or unsubstituted furanyl, substituted or unsubstituted benzofuranyl, substituted or unsubstituted thienyl or substituted or unsubstituted benzothienyl;

R<sup>9</sup> is hydrogen; and

R<sup>8</sup> is hydrogen.

The remaining claims currently under this rejection (*i.e.*, claims 3, 4, 29-36, 42, 43, 49-62, 66, 68, 70-80, 82, 84 and 85) are directly or indirectly dependent upon one of claims 1, 67, 69 or 81.

The Examiner stated that various substituents of the tetracycline ring structure, such as heterocyclic, aryl and heteroaromatic, are not enabled by the present specification. (*See* Office Action at p. 9). The Examiner also asserted that these substituents contain large numbers of heterocyclic substituents and, further, that there is no guidance or description to prepare and use the large number of compounds described. (*See* Office Action at p. 9). Finally, the Examiner alleged that the instant claims do not comply with the enablement requirement since one of ordinary skill would have to engage in undue experimentation to practice the invention. (*See* Office Action at p. 14). Applicants traverse the rejection.

Applicants believe that the term "arylalkyl" and not "alkylamino" was intended by the Examiner. "Alkylamino" does not require the inclusion of an aryl or cyclic group. (*See* Office Action at pp. 9-10). As such, the arguments below are made based on the assumption that the Examiner intended "arylalkyl" where "alkylamino" is used.

A considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

Applicants assert the ordinarily skilled artisan reading the instant claims in view of the specification would readily recognize how to make and use the invention without undue experimentation. Specifically, Applicants submit the scope of the pending claims and the guidance provided by the instant specification permit the skilled artisan to readily make and use the invention.

The present invention is drawn to methods and pharmaceutical compositions which comprise the use of specific, well-defined compounds of Formula (I) with 5-member heteroaryl rings at the 7-position and hydrogen at the 9-position to treat or prevent malaria. Several methods of making these compounds are described in the specification. (*See e.g.*, from p. 80, line 23 through p. 86, line 5 and Example 1 of the specification as filed). Furthermore, the

level of skill in the pertinent art is high. As such, Applicants submit that the skilled artisan would readily recognize how to utilize the procedures and compounds described in the specification to make and use the compounds of Formula (I), as amended, to practice the currently claimed methods.

Thus, based on the foregoing, Applicants submit that one of ordinary skill could make and use the present invention given the scope of the claims, the guidance provided in the specification, and the high level of skill in the art without engaging in undue experimentation. As such, the full scope of the instant claims is enabled. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

Applicants note that the pending claims do not recite a unit dose which is used to treat or prevent tumors, as alleged by the Examiner. (*See* Office Action at pp. 13-14). Thus, the Examiner's argument regarding the "how to use" prong of 35 U.S.C. §112, first paragraph, is moot.

#### **Double Patenting**

Claims 1, 3, 4, 29-36, 42, 43, 49-62, 66-82, 84 and 85 have been provisionally rejected on the ground of 35 U.S.C. §101 as claiming the same invention as that of claim 165 of U.S. Application No. 10/835,635.

Applicants believe this rejection is directed to U.S. Application No. 10/853,635, since U.S. Application No. 10/835,635 is drawn to an "apparatus and method for removing fine particles during fabrication of a portable camera module" and is not currently pending (*i.e.*, application has issued as US Patent No. 7,247,176).

Claim 165 of U.S. Application No. 10/853,635 (now allowed) is drawn to a tetracycline compound. However, the currently pending claims are drawn to methods and pharmaceutical compositions comprising the use of several tetracycline compounds. Claim 165 of U.S. Application No. 10/853,635 is drawn to a different statutory subject matter than that of the currently pending claims. Furthermore, claim 165 of U.S. Application No. 10/853,635 (now allowed) describes a tetracycline compound substituted with a phenyl ring at the 7-position. The current claims do not include 7-phenyl substituted tetracycline compounds. Thus, claims 1, 3, 4, 29-36, 42, 43, 49-62, 66-82, 84 and 85 do not claim the same invention as that of claim

165 of U.S. Application No. 10/835,635. As such, Applicants request withdrawal of this provisional rejection.

Claims 1, 3, 4, 29-36, 42, 43, 49-62, 66-82, 84 and 85 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 165 and 184 of copending U.S. Application No. 10/853,635; claims 109 and 115 of copending U.S. Application No. 10/996,119; and claims 1-5 of copending U.S. Application No. 12/351,409.

Applicants note that U.S. Application No. 12/351,409 is not publicly accessible on the USPTO website. Furthermore, this application is not accessible on Private PAIR. In fact, U.S. Application No. 12/351,409 is not a copending application which is assigned to the instant assignee, Paratek Pharmaceuticals, Inc. As such, Applicants request withdrawal of this provisional rejection.

With regard to U.S. Application Nos. 10/853,635 and 10/996,119, Applicants will consider filing terminal disclaimers upon a finding of allowable subject matter.

Claims 1, 3, 4, 29-36, 42, 43, 49-62, 66-82, 84 and 85 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-28 of copending U.S. Application No. 11/490,867. Applicants will consider filing a terminal disclaimer upon a finding of allowable subject matter.

Unspecified claims have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over copending U.S. Application Nos. 12/351,409; 10/921,580; 10/943,571; 10/996,119; 11/039,230; 11/348,608 and 11/490,867.

As described above, U.S. Application No. 12/351,409 is not a copending application assigned to the instant assignee, Paratek Pharmaceuticals, Inc. As such, Applicants request withdrawal of this provisional rejection.

With respect to U.S. Application Nos. 11/039,230; 11/348,608 and 11/490,867, Applicants traverse these provisional double patenting rejections. M.P.E.P. § 804 section I, subsection B1 provides as follows:

If a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed

application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer. If the ODP rejection is the only rejection remaining in the later-filed application, while the earlier-filed application is rejectable on other grounds, a terminal disclaimer must be required in the later-filed application before the rejection can be withdrawn.

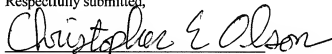
The instant application was filed on October 24, 2003. The cited co-pending Application Nos. 11/039,230; 11/348,608; and 11/490,867 were filed after October 24, 2003. Thus, the instant application is the earlier-filed application with respect to these applications. Accordingly, this provisional double patenting rejection should be withdrawn upon the favorable resolution of all other outstanding rejections.

With respect to Application Nos. 10/921,580; 10/943,571 and 10/996,119, Applicants will consider filing terminal disclaimers upon a notice of allowable subject matter.

#### **Conclusion**

Applicants submit that this paper is fully responsive and that the application is in condition for allowance. Should any questions arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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